

The opinion in support of the decision being entered today
is *not* binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte HARRY R. DAVIS,
TEDDY KOSOGLOU, and GILLES J. PICARD

Appeal 2007-0181
Application 10/057,323
Technology Center 1600

Decided: June 28, 2007

Before TONI R. SCHEINER, DONALD E. ADAMS, and LORA M. GREEN, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the Examiner's final rejection of claims 1-4, 11-13, 21, 28, 32, 34, 37-40, 42,

43, 47, 48, 83, 84, 86, 100, and 101.¹ We have jurisdiction under 35 U.S.C. § 6(b).

Claim 1, reproduced in the Appendix to the Appeal Brief, is representative of the claims on appeal and is drawn to a composition comprising a peroxisome proliferators-activated receptor (PPAR) activator and at least one sterol adsorption inhibitor. Appellants elected fenofibrate as the PPAR activator, and ezetimibe as the sterol absorption inhibitor (Br. 5).

The Examiner relies upon the following references:

Rosenblum US 5,846,966 Dec. 8, 1998.

The Medical Letter on Drugs and Therapeutics, 40 The Medical Letter, Inc.
1030:68-69 (1998).

Bertram G. Katzung, Basic and Clinical Pharmacology, 6th ed., 1995 at 529.

Claims 1-4, 11-13, 37-40, 42, 43, 47, 48, 83, 84, and 86 stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by the combination of Rosenblum and Medical Letter. Claims 21, 28, 32, and 34 stand rejected under 35 U.S.C. § 103(a) as being obvious over the previous combination as further combined with Katzung. Finally, claims 100 and 101 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Rosenblum and Katzung.

We affirm-in-part.

¹ Claims 1-4, 11-13, 21, 28, 32, 34, 37-40, 42, 43, 47, 48, 83, 84, 86, 100, and 101 are pending, and claims 5-10, 14-20, 22-31, 33, 35, 36, 41, 44-46, 49-82, 85, and 87-99 stand withdrawn from consideration as being drawn to a non-elected invention (Br. 1).

DISCUSSION

The Examiner rejected claims 1-4, 11-13, 37-40, 42, 43, 47, 48, 83, 84, and 86 under 35 U.S.C. § 103(a) as being obvious over the combination of Rosenblum and Medical Letter (Answer 4). As Appellants do not argue the claims separately, we focus our analysis on independent claim 1. Merely pointing out differences in what the claims cover is not an argument as to why the claims are separately patentable. 37 CFR § 41.37(c)(1)(vii).

Rosenblum is cited for teaching ezetimibe is useful for reducing cholesterol levels and the risk of atherosclerosis (Answer 4). Medical Letter is cited for teaching that fenofibrate is useful in reducing serum cholesterol levels (*id.*). The Examiner acknowledges that “[t]he references do not expressly teach a composition containing fenofibrate and ezetimibe together.” (*Id.*)

The Examiner concludes, however:

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate both ezetimibe and fenofibrate together in a single composition.

One of ordinary skill in the art would have been motivated to incorporate both ezetimibe and fenofibrate together in a single composition. The prior art teaches that both ezetimibe and fenofibrate are useful in reducing serum cholesterol individually. Therefore, combining two agents, which are known to be useful to reduce serum cholesterol individually, into a single composition useful for the same purpose is *prima facie* obvious (See *In re Kerkhoven* 205 USPQ 1069).

(Answer 4.)

The burden is on the Examiner to set forth a *prima facie* case of obviousness. See *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598-

99 (Fed. Cir. 1988). In order to determine whether a *prima facie* case of obviousness has been established, we considered the factors set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1996); (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the relevant art; and (4) objective evidence of nonobviousness, if present. We find that the Examiner has set forth a *prima facie* case of obviousness, and the rejection is affirmed.

Appellants argue that neither Rosenblum nor Medical Letter provides motivation for substituting a PPAR such as fenofibrate for the statin used in combination with the ezetimibe as taught by Rosenblum, as Medical Letter teaches at page 68 that fenofibrate is not as effective as the statins in lowering LDL cholesterol, a major risk factor in atherogenesis (Br. 9-10). Moreover, according to Appellants, “[t]here is no guidance provided by Rosenblum [] nor Medical Letter to pick and choose among numerous cholesterol treatments to select the particularly claimed combination of sterol adsorption inhibitor . . . (e.g., ezetimibe)[] and PPAR activator (such as fenofibrate).” (*Id.* at 10).

Rosenblum teaches that the disclosed compounds, such as ezetimibe, lower serum lipid levels, and in particular, serum cholesterol levels (Rosenblum, col. 20, ll. 39-40). The compounds “inhibit the intestinal absorption of cholesterol and . . . significantly reduce the formation of liver cholesteryl esters,” and are thus hypcholesterolemic agents, useful in the treatment and prevention of atherosclerosis (*id.* at ll. 42-48). In addition, Rosenblum teaches that the compounds of the invention, such as ezetimibe, may be administered in combination with a cholesterol biosynthesis inhibitor (*id.* at col. 21, ll. 26-28).

Medical Letter teaches that fenofibrate is used in the treatment of hypertriglyceridemia (Medical Letter 58). Fenofibrate increases lipoprotein lipase activity and triglyceride clearance (*id.*). In addition, Medical Letter teaches that fenofibrate decreases LDL cholesterol (*id.*).

It would have been obvious to one of ordinary skill in the art to combine ezetimibe as taught by Rosenblum with fenofibrate as taught by Medical Letter because both references teach that both compounds lower serum cholesterol levels. This type of motivation has been recognized often by the predecessor of our reviewing court, which has held that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the same purpose. *In re Susi*, 440 F.2d 442, 445, 169 USPQ 423, 426 (CCPA 1971); *In re Crockett*, 279 F.2d 274, 276-77, 126 USPQ 186, 188 (CCPA 1960). The idea of combining them flows logically from their having been individually taught in the prior art. *In re Kerkhoven*, 626 F.2d 846, 851, 205 USPQ 1069, 1072 (CCPA 1980). Here the art recognized property of each of the described agents as a cholesterol lowering agent would have provided one of ordinary skill in the art with ample suggestion of their combination in the composition as claimed. *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1739, 82 USPQ2d 1385, 1395 (2007) (“The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.”).

With respect to Appellants’ argument that neither Rosenblum nor Medical Letter provides motivation for substituting a PPAR such as fenofibrate for the statin used in combination with the ezetimibe as taught by

Rosenblum, as Medical Letter teaches at page 68 that fenofibrate is not as effective as the statins in lowering LDL cholesterol, a major risk factor in atherogenesis, we disagree. “A statement that a particular combination is not a preferred embodiment does not teach away absent clear discouragement of that combination.” *Syntex (USA) LLC v. Apotex, Inc.*, 407 F.3d 1371, 1380, 74 USPQ2d 1823, 1830 (Fed. Cir. 2005) (citations deleted). Moreover, the fact that the combination of ezetimibe and fenofibrate is one of a number of obvious combinations of cholesterol treatments does not make it any less obvious. *KSR*, 127 S.Ct. at 1742, 82 USPQ2d at 1397 (“What matters is the objective reach of the claim. If the claim extends to what is obvious, it is invalid under § 103.”).

Claims 21, 28, 32, and 34 stand rejected as being obvious over the combination of Rosenblum and Medical Letter as applied to claims 1-4, 11-13, 37-40, 42, 43, 47, 48, 83, 84, and 86 under 35 U.S.C. § 103(a) above, as further combined with Katzung (Answer 5).

Rosenblum and Medical Letter are relied upon as above (*id.*). Katzung is cited for teaching that niacin is also useful as a cholesterol lowering agent (*id.*). The Examiner concludes that it would have been obvious to combine niacin with the ezetimibe-fenofibrate composition taught by the combination of Rosenblum and Medical Letter because the combination of two or more agents, each known to be useful in reducing serum cholesterol, would have been *prima facie* obvious (*id.*).

As to claims 21 and 28, Appellants argue that neither Rosenblum nor Medical Letter suggest or provide any motivation for combining a sterol absorption inhibitor such as ezetimibe, a PPAR activator such as fenofibrate, and niacin (Br. 12). Appellants argue that the references provide no

teaching as to potential drug-drug interactions, and argue that Medical Letter at page 69 “discloses that it is unclear whether, *like gemfibril and niacin*, concurrent administration of fenofibrate with a statin could increase the risk of rhabdomyolysis.” (Br. 12 (emphasis in original).) Appellants assert that “[b]ecause of the difference of the way that each component of the presently claimed combination acts, it is respectfully submitted that the rejection is based upon an improper combination of references.” (*Id.*)

Claim 21, which we choose as representative of claims 21 and 28, is drawn to the composition of claim 1, further comprising niacin. As noted above, all three compounds are known to lower serum cholesterol, and for the reasons already set forth with respect to the rejection of claims 1-4, 11-13, 37-40, 42, 43, 47, 48, 83, 84, and 86, the art recognized property of each of the described agents as a cholesterol lowering agent would have provided one of ordinary skill in the art with ample suggestion of their combination in the composition as claimed.

We also do not find convincing Appellants’ arguments that the references provide no teaching as to potential drug-drug interactions, and that Medical Letter at page 69 teaches that it is unclear whether, like gemfibril and niacin, concurrent administration of fenofibrate with a statin could increase the risk of rhabdomyolysis. Medical Letter teaches that:

Like other fibrates, fenofibrate potentiates the effects of oral anticoagulants. Whether, like gemfibrozil and niacin, it could increase the risk of rhabdomyolysis when taken concurrently with a statin is unclear.

(Medical Letter 69).

Thus, the concern in Medical Letter is the combination of fenofibrate, gemfibrozil, or niacin with statins, but statins are not required by the

composition of claim 21. In addition, all that is required is a reasonable expectation of success, not absolute predictability of success. *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

As to claim 32, Appellants argue neither Rosenblum, Medical Letter, nor Katzung, taken alone or together suggests a triple combination treatment of a sterol absorption inhibitor such as ezetimibe, a PPAR activator such as fenofibrate, and at least one cardiovascular agent selected from the group of calcium channel blockers, adrenergic blockers, adrenergic stimulants, angiotensin converting enzyme inhibitors, antihypertensive, angiotensin II receptor antagonists, anti-anginal agents, coronary vasodilators, diuretics, and combinations thereof (Br. 13).

We agree with Appellants. Claim 32 is drawn to the composition of claim 1, further comprising “at least one cardiovascular agent selected from the group of calcium channel blockers, adrenergic blockers, adrenergic stimulants, angiotensin converting enzyme inhibitors, antihypertensive, angiotensin II receptor antagonists, anti-anginal agents, coronary vasodilators, diuretics, and combinations thereof.” The Examiner has made no findings as to the inclusion of any of the listed agents, and we are thus compelled to reverse the rejection. *KSR.*, 127 S.Ct. at 1741, 82 USPQ2d at 1396 (noting in order to facilitate review of the obviousness determination, the “analysis should be made explicit.”).

As to claim 34, Appellants argue neither Rosenblum, Medical Letter, nor Katzung, taken alone or together suggests a pharmaceutical composition for the treatment of a vascular condition, diabetes, obesity, or lowering a concentration of a sterol in plasma of a mammal, using the composition of claim 1 and a carrier (Br. 13).

The statement “for the treatment of a vascular condition, diabetes, obesity or lowering a concentration of a sterol in plasma of a mammal” is a statement of intended use and not a patentable limitation. Thus, all that is required is a composition as in claim 1 and a pharmaceutically acceptable carrier. Thus, as the combination of Rosenblum and Medical Letter render obvious a composition comprising ezetimibe and fenofibrate for lowering serum cholesterol levels, it would have been obvious to include a pharmaceutically acceptable carrier as the use of a pharmaceutically acceptable carrier is taught by Rosenblum and well known to the ordinary artisan. Thus, the rejection is affirmed as to claim 34.

The Examiner rejected claims 100 and 101 under 35 U.S.C. § 103(a) as being obvious over the combination of Rosenblum and Katzung (Answer 5). As Appellants do not argue the claims separately, we focus our analysis on claim 100.

Rosenblum is cited as above to the rejection of claims 1-4, 11-13, 37-40, 42, 43, 47, 48, 83, 84, and 86 under 35 U.S.C. § 103(a) as being obvious over the combination of Rosenblum and Medical Letter. That is, Rosenblum was cited for its teaching that ezetimibe is useful for reducing cholesterol levels and the risk of atherosclerosis (Answer 6). Katzung is cited for teaching that niacin is also useful for lowering cholesterol (*id.*). Thus, the Examiner concludes that it would have been obvious to combine niacin as taught by Katzung with the ezetimibe as taught by Rosenblum because the combination of two or more agents, each known to be useful in reducing serum cholesterol, would have been *prima facie* obvious (*id.*).

Appellants argue that “neither Rosenblum nor Katzung suggests or disclose combinations of a sterol absorption inhibitor and antioxidant or vitamin.” (Br. 14).

Claim 100 is drawn a composition comprising at least one antioxidant or vitamin, such as niacin, and a substituted azetidinone or substituted β -lactam compound or isomers thereof, such as ezetimibe. As noted above, both compounds are known to lower serum cholesterol, and for the reasons already set forth with respect to the rejection of claims 1-4, 11-13, 37-40, 42, 43, 47, 48, 83, 84, and 86, the art recognized property of each of the described agents as a cholesterol lowering agent would have provided one of ordinary skill in the art with ample suggestion of their combination in the composition as claimed.

CONCLUSION

In summary, we affirm the rejections of claims 1-4, 11-13, 37-40, 42, 43, 47, 48, 83, 84, and 86 under 35 U.S.C. § 103(a) as being rendered obvious by the combination of Rosenblum and Medical Letter; claims 21, 28, and 34 under 35 U.S.C. § 103(a) as being obvious over the previous combination as further combined with Katzung; and claims 100 and 101 under 35 U.S.C. § 103(a) as being obvious over the combination of Rosenblum and Katzung. Because the Examiner failed to make the findings necessary to support a *prima facie* case of obviousness as to the rejection of claim 32 under 35 U.S.C. § 103(a) as being obvious over the combination of Rosenblum and Medical Letter as further combined with Katzung, we are compelled to reverse the rejection as to that claim.

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No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED-IN-PART

smsc

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